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| EXAMINER |
|---|
| COUNTS, GARY W |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | 11 |

DATE MAILED: 01/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/972,882 | MENDEL-HARTVIG ET AL. | |
| | Examin r | Art Unit | |
| | Gary W. Counts | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the corr spond nce address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### Status of the claims

The amendment filed November 14, 2002 is acknowledged and has been entered.

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claim 1 is vague and indefinite because there appears to be a correlation step missing for the detection of the analyte. It is unclear how the analyte can be detected without the use of a label.

Claim 1, part (b) "specified fraction" is vague and indefinite. It is unclear what is considered to be a specified fraction, i.e. all of the receptor or a percentage of the amount of receptor (4/4 can be considered a specified fraction). There is no definition of the term provided in the specification. See deficiencies throughout the claims.

Claim 1, part (d) "the concentration" there is insufficient antecedent basis for this limitation.

Claim 5 is vague and indefinite because it is unclear if the receptor-binding capacity of the solid phase is directed to the same target as the solid phase binding capacity of receptor contacted with the sample. Claim 5 has not been treated on art. However, if applicant should amend the claim any art rejection will be made FINAL.

Claim 31 "said flow matrix" there is insufficient antecedent basis for this limitation.

Claim 33 "the receptor-binding capacity" and "the analyte-specific receptor substance" there is insufficient antecedent basis for these limitations.

Claim 34 "the receptor-binding capacity" and "the ligand-binding capacity" there is insufficient antecedent basis for this limitation.

Claim 37 "the range" there is insufficient antecedent basis for these limitations.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1, 4, 6-8, 10, 13, 14, 15, 22, 25 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Forrest et al (EP 0105714).

Forrest et al disclose a method for determining an analyte in a sample. Forrest et al disclose that the method employs the "sandwich" technique involves the use of an excess amount of receptor to the analyte. Forrest et al disclose contacting the sample with labeled antibodies to the antigen (analyte) and a reagent comprising antibodies to the antigen (analyte). Forrest et al disclose immobilized reagents on a solid phase support, separating the solids fraction from the liquid fraction and determining the amount of label in one of the said fractions and, therefrom, the amount of antigen present in the sample (pages 4 and 5) (page 12). Forrest et al disclose that the labeled antibody reagent can carry a chromophore (p. 9, lines 20-21). Forrest et al disclose that the solid support may take the form of particles, beads, wall-coatings on the reaction vessel or an insert of large surface area (abstract). Forrest et al also disclose the use of a kit (page 10). Forrest et al disclose that the labeled and unlabelled antibody reagents may be added in any order, or simultaneously (p. 9, lines 11-17).

6. Claims 1-3, 8-10,13, 14, 16, 17 rejected under 35 U.S.C. 102(e) as being anticipated by Neumann et al (US 6,184,042).

Neumann et al disclose a method for the immunological determination of an analyte in a sample. Neumann et al disclose the use of a heterogeneous sandwich assay in which the soluble antibody and the solid phase antibody are present in an excess relative to the analyte to be determined so that the sandwich complexes can be formed and also detected essentially completely (col 1, lines 35-44). Neumann et al

disclose incubating the sample liquid in the presence of a solid phase with at least two receptors capable of binding to the analyte to be determined in which the first receptor is soluble and the second receptor is bound to a solid phase or is capable of binding to a solid phase and the analyte is detected by determining the label in the solid phase or in the liquid phase. Neumann et al disclose that the solid phase is isolated from the liquid phase (col 4, lines 45-55). Neumann et al disclose that the first receptor is an oligomeric antibody or antibody fragment. Neumann et al disclose that the use of this oligomeric antibody reduces the Hook effect and thus allows for the sample to have a high concentration of analyte and allows for performing the assay on undiluted samples (col 1, line 36 – col 2, line 46). Nuemann et al disclose that the first receptor (antibody) comprises a detectable label (col 3, lines 1-27). Neumann et al disclose that the sample is a serum sample (col 7, line 39). Neumann et al disclose that the second receptor is bound to the solid phase and that the second receptor is biotinylated and the solid phase is coated with avidin or streptavidin (col 4, lines 17-19).

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 11, 12, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neumann et al (US 6,184,042) in view of Nazareth et al (US 6,319,676).

See above for teachings of Neumann et al.

Neumann et al differ from the instant invention in failing to teach the solid phase binding sites for the receptor are immobilized in a reaction zone of a flow matrix.

Nazareth et al disclose a lateral flow matrix using the sandwich technique in which receptors are immobilized in the reaction zone of the flow matrix (col 1- col 4). Nazareth also disclose predeposited analyte-binding receptor reagent upstream of the reaction zone (col 2, lines 29-52). Nazareth et al disclose the use of immobilized receptors in the flow matrix provides for a rapid, sensitive device and method for detecting the presence of analytes in body fluids and that the method and device have high sensitivity and result in virtually no false positives (col 1, lines 44-50).

It would have been obvious to one of ordinary skill in the art to immobilize the receptors to a solid phase such as taught by Nazareth et al into the method of Neumann et al because Nazareth et al shows that the use of immobilized receptors in the flow matrix provides for a rapid, sensitive device and method for detecting the presence of analytes in body fluids and that the method and device have high sensitivity and result in virtually no false positives.

With respect to the ratios between said isolated fraction of the amount of active analyte-binding receptor ant the total amount of active analyte-binding receptor contacted with the sample and the range values as recited in the instant claims, the optimum ratio and range can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result

effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Neumann et al in view of Guan et al. ( US 6,316,205).

See above for teachings of Neumann et al.

Neumann et al differ from the instant invention in failing to teach the sample is a whole blood sample.

Guan et al disclose a sandwich assay in which the sample is a whole blood sample. The use of such a sample provides for a versatile assay device (col 5, lines 13-29).

It would have been obvious to one of ordinary skill in the art to use a whole blood sample as taught by Guan et al into the method of Neumann et al because Guan et al shows that the use of such a sample provides for a versatile assay device.

10. Claims 19-28 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neumann (US 6,184,042)et al in view of Nazareth (US 6,319,676) and Boguslaski et al (US 5,420,016).

See above for teachings of Neumann et al and Nazareth et al.

Neumann et al and Nazareth et al differ from the instant invention in failing to

disclose packaging the components into a kit.

Boguslaski et al disclose assembling various system components into a test kit. By assembling these components into test kits, it makes it more convenient and facile for the test operator (col 7, lines 8-11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to assemble the various reagents and components of Neumann et al and Nazareth et al into kits such as taught by Boguslaski et al because Boguslaski shows that test kits make it more convenient and facile for the test operator. Furthermore, with respect to the ratio between the amount of ligand-binding analyte-specific receptor and the total amount of analyte-specific receptor as recited in the instant claims, the optimum ratio can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

***Response to Arguments***

11. Applicant's arguments filed November 14, 2002 have been fully considered but they are not persuasive.

Applicant argues that the assays of the references use a mixture of solid phase bound and free receptor, whereas the present invention uses only one receptor type. Applicant specifically refers to column 2, lines 26-31 of U.S. '042. It is noted that the references use a mixture of solid phase bound and receptor. However, the comprising language as recited in the claims would include the inclusion of other components. Unless there is a recitation in the claims which excludes other components, the claim as recited encompasses the teachings of the prior art of record. Applicant further argues that claim 1 further recites the sequential binding of affinity reagents, as indicated recitation of "steps" a) and b). This is not found persuasive because the use of comprising language in the method allows steps to be carried out in any order. Furthermore, Forrest et al disclose that the labeled and unlabeled antibody reagents may be added in any order or simultaneously.

Applicant argues that the present invention isolates a specified fraction of the receptor, with or without bound analyte. As disclosed in the previous office action and reiterated in this office action. It is unclear what is considered to be a specified fraction (see 112 rejection above). Therefore it is the Examiner's position that the Forrest et al reference and the Neumann et al references still read on the claims as recited.

Applicant argues that the present invention is distinguished from the primary references and that the combination of the secondary references with the teachings of

the primary references (Forrest et al and Neumann et al) would not achieve the present invention. It is Examiner's position that the primary references still read on the claims as recited and therefore the combination of the secondary references with the primary references is appropriate.

***Conclusion***

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
January 13, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
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01/24/03